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The Effectiveness of Needle Exchange Programmes for HIV Prevention - A Critical Review

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Abstract:

HIV transmission by contaminated needles and syringes among injecting drug users (IDUs) is one of the three main modes of transmission that fuel the HIV pandemic. Needle exchange programmes (NEPs) were adopted to reduce HIV transmission in this risk group. The aim of this review was to investigate evidence for the effectiveness of NEPs.

Literature searches were conducted covering articles published until December 2005. In the final selection only studies using HIV incidence or prevalence data as outcome variables were included. Nine studies presented data addressing the effect of NEPs on HIV incidence. Seven of these studies showed no significant effect, one showed a positive and one an unfavourable effect. Three looked at HIV prevalence at baseline, all showing an unfavourable effect. The method used in three ecological studies that investigated changes in HIV prevalence in cities with and without NEPs have drawbacks, and the results should not be used as evidence for the effectiveness of NEPs.

The effectiveness of NEPs to prevent HIV transmission among IDUs is overrated in previous reviews. The conclusion that NEPs are the superior method for preventing HIV transmission among IDUs may have delayed the implementation of more effective and integrated methods.

Introduction

It is estimated that approximately 10% of all persons living with HIV world-wide have been infected through drug injection (1). In some regions, especially in Southeast Asia and Eastern Europe, this is at present the primary transmission route (1). Therefore, it is important that the HIV prevention strategies for injecting drug users (IDUs) are well-founded and effective. In chapter 4 of the World Health Organization (WHO)'s *Policy and programming guide for HIV/AIDS prevention and care among injecting drug users*, Needle Exchange Programmes (NEPs) are emphasized as one of the most effective interventions to date in preventing HIV transmission (1). Needle exchange is indeed the measure that has come to be very widely promoted and used all over the world (2,3).

A number of reviews of the NEP literature have been conducted. Some of these have looked specifically at the effects of needle exchange while others have investigated HIV prevention measures in general (4,5,6,7,2,8,9,3,10,11). These reviews have all concluded that NEPs are useful for preventing the spread of HIV because they reduce risk behaviour among IDUs.

Only the two most recent reviews (2,11) had the explicit aim of systematically scrutinising all available studies. Both of these reviews, to some extent, lack a thorough discussion of the relevance of methods, the authors' conclusions and the conflicting results. These shortcomings are greater in the review published by the WHO (11), later published in *Substance Use and Misuse* (12), more so than Gibson et al. (2) Gibson et al. (2) accepts the results in studies where authors report positive findings but also makes note of design problems and lack of inclusion of possible confounders in these studies. On the other hand, it is sceptical towards the results of studies in which null or negative findings are reported and tries to find plausible explanations for the lack of positive findings. This is a biased approach. Wodak and Cooney (11,12) do not discuss the positive findings in studies where HIV incidence/prevalence is the outcome variable. A critical evaluation of this review is warranted.

The focus of this review is on studies addressing the effectiveness of NEPs to prevent HIV using either HIV incidence or prevalence as outcome variables, variables that are more reliable outcomes than self-reported risk behaviour. These articles are scrutinized in a way that was lacking in two previous reviews (2,11,12). The present review provides a supplementary basis necessary for discussing the evidence of NEPs as the best way of reducing HIV transmission among IDUs.

Method

A literature search was carried out during February 2004 to December 2005, covering articles published until December 2005. A MEDLINE and PsycINFO search for both keywords and MESH headings identified 103 articles. The keywords were "needle exchange and injection drug use" and "syringe exchange and injection drug use".

An additional 71 articles were found in the reference lists of the initial 103 papers, yielding a total of 174 articles that addressed NEPs. These articles were tested against the following two criteria: (1) the study attempted to measure the effects of needle exchange and (2) the study contained control and/or comparison groups to test the effects of needle exchange. A total of 69 articles met these two inclusion criteria. All studies that did not include measurement of HIV incidence or prevalence as outcome were excluded. Thirteen studies remained and were the basis for the present review (13,14,15,16,17,18,19,20,21,22,23,24,25). Three additional studies were also included (26,27,28) in order to be able to discuss the HIV incidence/prevalence outcome as presented in the review by Wodak and Cooney (11,12). The Australian report, Health Outcome International (27), appears to be based on (almost) the same data as the article by MacDonald et al. (17)

Results

Fourteen studies attempted to measure the effect of needle exchange on the incidence or prevalence of HIV. See Table 1.

Studies in single cities

Amsterdam

The first study is from Amsterdam and was published in 1992 (25). HIV-incidence in a cohort was studied as a case-control study. The NEP started in 1984, and the study covers the years 1986-1991. Factors significantly associated with HIV seroconversion in the multivariate analysis were: having lived for more than 10 years in Amsterdam, having injected for the first time less than two years before inclusion in study and injecting mainly at home (protective factor). Attending the NEP did not predict or protect from seroconversion. In a follow up study (9) HIV incidence was not used as an outcome variable, but the authors concluded that in spite of a wide variety of harm reduction measures in Amsterdam, including several NEPs, HIV incidence did not continue to fall below 3-4% after 1991. The main suggestion for alternative intervention was injection prevention and promotion of cessation of injection, but also a shift from passive availability of HIV testing and counselling service to a more active policy, since HIV-positive IDUs reduce risk behaviour to a larger extent than HIV-negative IDUs in this study.

New York City

Perhaps one of the most quoted studies (15), a meta-analytic study pooling data from three different studies in New York City, demonstrated a significantly lower HIV-incidence among NEP-users than for the control group. While HIV seroprevalence at all sites was approximately 50%, the peak of the epidemic had passed. All NEP-users were from two smaller studies conducted in 1992-94 and 1995, whereas the majority of non-users were from a larger study performed during 1988-91. The non-users from this older study had the highest incidence, 6.23 per 100 person years (PY) (CI 4.38-8.60). Non-users in the later study also had a high incidence, 5.26 per 100 PY (CI 2.41-11.49) compared to 1.58 (CI 0.54-4.65) and 1.38 (CI 0.23-4.57) among NEP-users in the two later studies. In the multivariate analysis the authors controlled for sex, age and frequency of injection and concluded that not using NEPs had an adjusted hazard ratio of 3.3 (CI 1.3-8.7).

The Bronx, New York City

Schoenbaum et al. (22) conducted a prospective study from 1985-93 on patients using methadone with access to NEPs from 1989 in the Bronx, New York City. HIV infection was detected in 52.2%, and the prevalence was higher among NEP-users (58.1%) than non-users (50.5%) (p=0.06). Among those who were HIV-negative at entry, the seroconversion rate did not differ significantly between NEP-users and nonusers (1.77 vs. 1.69 per 100 PY) during follow-up. NEP attendance was independently associated with HIV seropositivity in a multivariate analysis of participants from 1989-1993 (Adjusted OR 1.39, 95% CI 1.00-1.94).

Vancouver

Three studies addressed the rapid increase of HIV among IDUs in Vancouver, Canada, that started in September 1994 (20,21,23). NEPs were established in Vancouver in 1988 and were considered the largest in North America, handing out millions of needles and syringes. At the time of NEP introduction the HIV seroprevalence was 1-2% among IDUs in Vancouver. Strathdee et al. (23) studied 1006 IDUs in 1996 -97. Baseline HIV seroprevalence was 23.2%, and 58% of persons with HIV infection were aware of their serostatus. Twenty-four seroconversions during follow-up yielded an incidence of 18.6 (95%CI 11.1-26.0) per 100 PY. Multivariate logistic regression of predictors of HIV-positive serostatus at baseline produced the following significant predictors: unstable housing, low education, commercial sex, borrowing used needles, injecting with others, established injector (injected >2 years) and frequent NEP attendance (more than once per week). It is also noteworthy that 23 of the 24 seroconverters reported NEPs as their most frequent source of sterile syringes, and only five reported having any difficulty obtaining sterile syringes. Patrick et al. (20) performed a case-control study including 89 IDUs with an initial HIV positive test after January 1, 1994, and a negative test within the prior 18 months as cases, and 192 controls with two negative tests during the same period. Behaviour in the inter-test interval was compared and analysed. All but 4 subjects had used one of the two local NEPs at least once. A majority, 66% of cases and 74% of controls, reported no current difficulties in obtaining sterile needles. Cases and controls reported re-using syringes a mean of 4.4 and 4.5 times, respectively. In the univariate analysis cases used NEPs significantly more often than controls (65% of cases vs. 52% of controls used NEPs daily to weekly), but in

the multivariate analysis the difference was no longer significant. The significant factors were: borrowing syringes, unstable housing and injecting four or more times daily as risk factors, and sex with opposite gender and cannabis use as protective factors. Finally, Schechter et al. (23) conducted a prospective cohort study of 694 HIV- negative IDUs in the same city starting in 1996-97. Frequent NEP users were defined as visiting NEPs at least once a week at baseline. Of the 505 frequent NEP users, 47 (11.8%) seroconverted compared to 17 (6.2%) of the infrequent users, a difference that was significant (log-rank test in Kaplan Meier plot, p=0.012). As in the previous study by Patrick et al. (20), frequent NEP use was no longer significant when other stronger risk factors were entered in the multivariate analysis. These factors were: unstable housing, hotel living, injecting four or more times a day, cocaine injecting at least once a day, Downtown Eastside as main injecting site and needing assistance when injecting.

Montreal

Bruneau et al. (14) reported results of a study conducted in Montreal. From September 1988 to January 1995, 1599 IDUs were enrolled with a baseline HIV seroprevalence of 10.7%. NEP use was defined as having obtained clean equipment at least once in the last six months from a NEP. Seroprevalence among NEP users was 16% compared to 5.8% among non-users. NEP use was a significant predictor of HIV seropositivity also when all relevant confounders were controlled for (adjusted Odds Ratio 2.2, 95% CI 1.5 -3.2). A total of 974 HIV seronegative IDUs who could be reached for follow up were included in an incidence study. The overall incidence was 5.1 per 100 PY (7.9 for NEP users, 95% CI 4.1-6.2 and 3.1 for non-users, 95% CI 2.1-4.4). NEP use remained significantly predictive for seroconversion when confounders were controlled for. Finally, a case-control study was performed using the 88 seroconverters as cases with 320 matched controls. NEP use was divided into exclusive or nonexclusive use in which the exclusive participants received all their needles from a NEP. There was elevated risk for seroconversion among both exclusive and non-exclusive NEP users also after adjusting for confounders.

Baltimore

Valente et al. (24) in 1994-97 studied 2574 NEP users in Baltimore and, in particular, investigated HIV seroconversion in a subsample of 262 IDUs. While NEP use was not significantly predictive (OR=1.18, CI 0.65-2.15 in bivariate analysis), a certain behaviour called syringe relay (defined as only returning syringes originally issued to someone else) was highly predictive for seroconversion among women but not among men. It was a small sample with only 12 seroconversions, but the authors suggest that the personal contact with NEP staff may be an important protective factor.

Studies including several cities/countries

Worldwide inclusion

Two articles compared changes in HIV seroprevalence in a number of cities with and without NEPs (16,17). In addition, a report (27) using the same design and almost the same data was included in a study by Wodak and Cooney (11,12). These studies estimated the change in HIV seroprevalence by using various regression techniques based on measurements of seroprevalence from at least two calendar years. Hurley et al. (16) studied 81 cities (29 with and 52 without NEPs); MacDonald et al. (17) 99 cities (36 with and 63 without NEPs); and in HOI (27) 103 cities were included (36 with and 67 without NEPs). It is possible that the two last studies include the cities in the first study. Hurley et al. (16) found an average increase per year of 5.9 % in cities without NEPs and an average 5.8 % decrease per year in cities with NEPs, yielding an annual change in seroprevalence that was 11 % lower (95 % CI 3.9 -17.6) in cities with NEPs. The corresponding figure in MacDonald et al. (17) and in HOI (27) was 24.7% (95 % CI - 0.5 - 43.8) and must cover much of the same material. This result was significant at the 10 % level (p=.06). All three studies also investigated a subgroup of cities with an initial HIV prevalence of 10 % or less and with sero-surveys over a period of at least three years. For this subgroup they reported different results: Hurley et al. (16) a non-significant result, MacDonald et al. (17) a significant (95 %) weighted mean difference of 18.4 % (p=0.03) and HOI (27) a non significant un-weighted mean difference of 25.3 % (p=0.20).

Six US cities

Monterosso et al. (17) included 3773 participants from 6 US cities and a women's correctional facility in 1994-1996 and interviewed and tested at baseline and follow-up after a mean time of 7.8 months. Among HIV seropositive at baseline (13%) the factors with highest relative risks were: knowingly having had a HIV -positive sex partner, being a homo- or bisexual man, having injected with HIV-positive IDUs, having injected for 10 or more years, having traded sex for money or drugs and having started injecting before age 25. At follow up a total of 19 new cases were found in 5 cities. Two protective factors were identified, namely reduction of injection frequency and not using previously used needles at the time of any visit. NEP use was not significantly protective at the 5% level.

Nine Ontario cities

Millson et al. (18) conducted a study with 551 participants in 9 cities in Ontario in 1997-98. The HIV prevalence varied from 1.4% to 14.7% in the different cities. In logistic regression, HIV seropositivity was significantly associated with city of residence, injecting for more than 5 years, cocaine or crack use, injecting more than10 times a day and being a long term NEP user (OR 4.16, CI 1.45-11.97). An interesting finding in this study was that HIV-positive participants who reported knowing that they were HIV -positive were significantly more likely to report always using condoms (10/12) when compared to HIV-positive persons who did not know their true HIV status (1/9).

Three Scandinavian countries

Finally, Amundsen et al. (13) compared official estimates of IDU populations and estimates of HIV incidence based on registered data of new HIV infections among IDUs in Denmark, Norway and Sweden using a method of back calculation for the years 1991-96. The three countries had a similar outbreak of HIV among IDUs in the capital cities in the mid 1980s but adopted different strategies to combat the epidemic. In Norway and Denmark needles and syringes were legally easy to access, whereas in Sweden all sale and distribution of needles and syringes was illegal except at two experimental sites in the south of the country. In Norway and Sweden HIV testing and counselling was promoted, whereas in Denmark after 1987 there was a decline in the promotion of HIV testing among IDUs, and IDUs were less willing to accept testing. Incidence rates were lower and decreasing in Sweden (0.77-0.58/1000 IDUs) and Norway (0.92-0.58/1000 IDUs), whereas in Denmark the rate was stable at a higher level (1.49/1000 IDUs) in 1991-96. Even though the authors emphasize that the study is not conclusive, these results would indicate that testing and counselling may be more effective in preventing HIV among IDUs than NEPs.

Additional studies from the WHO review

The two following studies were included in Table 3a in the WHO review (11). Their design did not include a proper control group.

New Haven, Connecticut

Heimer et al. (26) reported from a legal NEP in New Haven, Connecticut, that was started in November 1990. By measuring HIV-DNA in returned syringes it was demonstrated that the prevalence of HIV-DNA in these samples dropped from an initial 63.9% to a steady rate of 42.8% in 5 months. The authors concluded that the main reason for this reduction was that the mean circulation time for each needle decreased. No data on seroprevalence in the IDU population was reported.

Lund, Sweden

Ljungberg et al. (28) reported on the first three years of a trial NEP in the small city Lund in the south of Sweden that started in November 1986. Despite very high HIV testing uptake, only four cases of HIV among IDUs were known in the area by 1987 (two infected in Stockholm, two abroad). No new cases were found by 1990, indicating that there was no epidemic among IDUs in the Lund area at this time. This situation was compared with Stockholm (the capital) where a rapid spread of HIV occurred among heroin injectors 1983-1985, resulting in a seroprevalence of 45-60% in 1987-1988. However, the annual incidence in Stockholm at that time was only about 1% without NEPs. The authors point out that their study cannot show any causal effect of NEPs based on the fortunate epidemiological situation. They also mention that one possible factor for the good situation may have been the influence of NEPs on the sharp increase in HIV testing.

Discussion

Results

Outcomes and effects

Generally, HIV seroincidence is regarded as the most relevant effect measure of NEPs on HIV prevention. In this review most studies on seroincidence concluded that the effect of NEPs was not significant (13,17,20,21,22,24,25). One showed a protective effect (15), and one showed NEP users to be at higher risk for HIV seroconversion than non-users (14). Four studies (14,18,22,23) investigated seroprevalence at baseline, all four showing a unfavourable situation for NEP users. In Schoenbaum et al. (22) NEP attendance was also independently associated with HIV seropositivity, but most of the HIV-positive participants were infected before NEPs were established. Three studies (27,16,17) looked at changes in seroprevalence, and all found a protective effect in the whole sample, the two last studies (17,27) at the 10 % level (p=0.06). Looking at a subsample, the two last studies disagreed on method (weighted vs. un-weighted analysis), and one found a protective effect (17) while the other found no protective effect (27).

Control for confounders

The study by Des Jarlais et al. (15) provides a strong case for the role of NEPs in the prevention of HIV. However, the factor of homelessness, which in other studies seems to have high impact on seroconversion, was not included in the multivariate analysis. Neither were any other services than needle exchange mentioned as offered at NEPs, nor to what extent IDUs in populations were HIV tested. In addition, it is not an optimal design to study users of NEPs in another calendar period than most of the non-users. Changes over time in HIV seroincidence and prevalence due to other factors than NEPs may have distorted the results.

The studies of Hurley et al. (16), MacDonald et al. (17) and HOI (27) using an ecological design at first glance present a strong argument for NEP effectiveness. But there are some serious problems with these studies (29). The studies did not control for a highly probable important confounder: the stage of the epidemic among IDUs. A careful reading suggests that weaknesses of the design and the measurements regarding the strength in the conclusions in favour of NEPs were not properly addressed. In most cities with a major HIV epidemic and NEPs, NEPs were introduced after the rapid increase phase and were thus typically associated with a stable or decreasing seroprevalence. There are some exceptions such as Vancouver and Amsterdam where NEPs were introduced before the peak. In these cities the prevalence increased despite NEPs (20,21,23,25). Some of the measurements from cities with epidemics but without

NEPs were conducted during the phase of rapid increase, since such an increase would tend to cause alarm in the community and an awareness of the importance of surveillance. The studies did not include information on other prevention measures present.

Antibody testing is a normal strategy in combating epidemics of viral and bacterial infections. The stigma attached to HIV has hampered the surveillance of epidemics and the possibilities for health services and infected persons to take proper action. Knowledge of one's positive HIV status may reduce risk behaviour (13,30,31,32,33,9) but among IDUs the results are fairly mixed (34,2,35) perhaps because drug injection is also stigmatising. HIV testing may, however, be part of NEPs and possibly interfere with effects of needle exchange. Amundsen et al. (13,29) actively discuss this, and Millson et al. (18) mentioned it briefly.

Review weaknesses

Since the report by Wodak and Cooney (11) was published by the WHO, it is taken especially seriously in governmental decision making. It is surprising that although all of the above studies, particularly those from Vancouver and Montreal (14,20,21,23), are mentioned in the review, they conclude with a strong recommendation for NEPs in the fight against HIV among IDUs. A further look at chapter three of their report in which the authors discuss studies with HIV incidence or prevalence as outcome variables reveals that the basis for their conclusion is even weaker. Compiling the information presented in Tables 3a, 3b and 3c, they find six studies in favour of NEPs as an effective means to prevent HIV, three negative and two that are inconclusive. A closer look at the six in favour reveals that the Monterosso et al. (19) study was misclassified as positive and should be moved to the group of inconclusive studies. The same holds for the study by Ljungberg et al. (28), based on the authors' own judgement of the epidemic situation in the region and later evaluations of the experimental NEPs in the south of Sweden. Two of the studies rated in favour should be reanalysed (27,16), taking into account the stage of the epidemic and possibly the level of known seropositive status. The data in Hurley et al. (16) are most likely included in the studies by MacDonald et al. (17) and HOI (27) and should possibly be addressed as a single study. A fifth study mentioned in favour, Heimer et al. (26), does not measure HIV prevalence in a population of IDUs, but in returned syringes and does not have a control group design. It is questionable whether the decrease in prevalence in the returned needles can be transferred to the IDU population. Thus, the original six studies rated in favour of NEPs appear to be much weaker.

Difficulties evaluating NEPs

There is really only one study (15) which has a strong case in favour of NEPs being an effective protection against HIV seroconversion among IDUs. However, the design of this study is not optimal. The ecological studies of cities with and without NEPs that are often cited as ultimately positive are questionable and should be reanalysed. The other studies indicate that NEPs usually make no difference. When NEPs appear to have an unfavourable effect, this may be due to the fact that frequent and high risk injectors tend to visit NEPs more often. Other possibilities for unfavourable outcomes may be that NEPs have not been designed well or that local factors have counteracted possible favourable effects. The situation in Vancouver, Canada, where three studies showed unfavourable outcomes (20,21,23) is summarized and discussed in a recent editorial (36). When the Vancouver HIV outbreak occurred, the NEP operated on a strict one-for-one syringe exchange policy, and hours of operation were restricted to daytime in an effort to reduce drug use in the vicinity of the exchange at night. Other factors are also referenced and described - including the large extent of high-intensity cocaine injectors and police crackdowns driving IDUs off the streets - that may have contributed to frequent sharing of needles and syringes even for persons who visited the NEP at daytime. While such factors are important for understanding unfavourable results of NEP use, they do not change, for example, the results of the three Vancouver studies into favourable outcomes. On the other hand, the lack of evidence of effectiveness of NEPs to prevent HIV does not mean that an opposite conclusion can be drawn: that NEPs enhance transmission of HIV. The partly contradictory results of studies addressing the effect of NEPs on the HIV epidemic may in part be due to the fact that NEP efforts can be very different despite the common task of handing out needles and syringes. The possible selection of high risk IDUs attending NEPs over time should be addressed in the design and analysis of studies.

Supplies of sterile equipment

It is better for a person using illicit drugs to inject with sterile equipment. However, it does not automatically follow that society has to provide sterile equipment. IDUs operate on an illegal market and tend to be quite skillful in providing what is needed for their habit in one way or another. The local situation for access to equipment should be understood before NEPs are established, and such action should be seen in context with other necessary measures. The offer of free needles and syringes will be appreciated if it is reasonably convenient. This establishes an opportunity to offer in an integrated way other preventive measures such as HIV testing and counselling, hepatitis A and B vaccination, birth control, dental care and other health and social care measures badly needed by IDUs (30,32).

Other outcomes

The initial approach for this review was to evaluate what is known about the effects of NEPs by means of a systematic scrutiny of all articles on the topic published in indexed academic journals. However, the studies looking at the effect of NEPs on self-reported risk behaviour without any biological marker used several different definitions. In our opinion these studies presented a very confused and contradictory picture. New, well-designed studies are warranted.

Shortcomings of our study

Our aim was to compile all the articles published in indexed, scientific journals. One shortcoming is that interesting findings published elsewhere are not included in our survey. It is also possible that articles fulfilling the criteria of being published in a scientific journal have been missed or accidentally excluded in the screening process even though our aim was to include all studies we found in reference lists, previously published reviews of the literature and in other published articles.

Conclusion

The effectiveness of NEPs to reduce HIV among IDUs is overrated. Errors in categorising studies in favour of NEPs have been made (11,12), and studies claiming positive results have not been adequately scrutinized. Based on the present review, recommending NEPs (along with substitution treatment) as the major strategic method for combating the highly alarming spread of HIV among IDUs in Eastern Europe and Southeast Asia as is done in official documents (37,1) is not correct. In the WHO guide for prevention and care for HIV/AIDS among IDUs (38), the conclusion that NEPs are superior to other measures is not based on solid evidence. This may have delayed the implementation of more effective and integrated tools.

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